

**AMENDMENTS TO THE CLAIMS:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**LISTING OF CLAIMS:**

Claims 1-18 (Canceled).

Claim 19 (Currently Amended): A method for purifying adenoviral particles from a crude viral preparation containing said adenoviral particles, comprising:

i) a fluidized bed chromatography step comprising at least the steps of:

- a. contacting said crude viral preparation with particles of adsorbent in fluidized bed under suitable conditions to allow adsorption of said adenoviral particles onto said particles of adsorbent,
- b. eluting the adsorbed adenoviral particles from said particles of adsorbent; and
- c. collecting the eluted adenoviral particles;

wherein said particles of adsorbent comprise an agarose matrix and a central core comprising quartz, and dextran chains covalently coupled to said agarose matrix, on which are attached positively charged groups; ~~and wherein the yield of adenoviral particles collected at step (c) is 80% or higher;~~ and,

ii) a gel filtration chromatography step that is carried out on a support comprising ~~beads with a diameter of between 5 and 105  $\mu$ m~~ an alkyl dextran and methylene bisacrylamide matrix or an ethylene glycol and methacrylate matrix.

Claim 20 (Previously Presented): The method as claimed in claim 19, wherein said agarose matrix is a 6% cross-linked agarose matrix.

Claim 21 (Previously Presented): The method as claimed in claim 20, wherein said positively charged groups are Q groups.

Claim 22 (Previously Presented): The method as claimed in claim 19, wherein said particles of adsorbent are of heterologous sizes.

Claim 23 (Currently Amended): The method as claimed in claim 19, wherein said positively charged groups have the formula  $[[R-CH(OH)-CH_2-N^+-(CH_3)_3]]$   $R-CH(OH)-CH_2-N^+-(CH_3)_3$ .

Claim 24 (Previously Presented): The method as claimed in claim 19, wherein said contacting step is carried out under pH conditions of between approximately 7.5 and approximately 9.5.

Claim 25 (Previously Presented): The method as claimed in claim 24, wherein said pH is approximately 8.5.

Claim 26 (Previously Presented): The method as claimed in claim 19, wherein said contacting step is carried out in a buffer equilibrated at a final NaCl concentration of 400 mM.

Claim 27 (Previously Presented): The method as claimed in claim 19, wherein said contacting step (c) is carried out under conductivity conditions of between approximately 25 and approximately 70 mS/cm.

Claim 28 (Previously Presented): The method as claimed in claim 27, wherein said conductivity conditions are between approximately 30 and approximately 40 mS/cm.

Claim 29 (Previously Presented): The method as claimed in claim 28, wherein said conductivity conditions are between approximately 30 and approximately 35 mS/cm.

Claim 30 (Previously Presented): The method as claimed in claim 19, wherein said eluting step is carried out by modifying the salinity or the pH used in the contacting step.

Claim 31 (Previously Presented): The method as claimed in claim 30, wherein said eluting step is carried out by increasing the salinity.

Claim 32 (Previously Presented): A protocol for producing adenoviral particles which can be used for gene therapy, comprising the following steps (i) and (ii);

- (i) producing a crude viral preparation, comprising:
  - (a) infecting or transfecting a suitable cell line with at least one adenoviral vector of interest;
  - (b) culturing said infected or transfected cell line under conditions which allow viral replication and the production of viral particles;
  - (c) collecting the cells and/or the supernatant,

(ii) purifying said adenoviral particles from crude viral preparation obtained at step (i)(c) according to the method of claim 19.

Claim 33 (Previously Presented): The protocol as claimed in claim 32, further comprising:

- (i) a cell rupture or lysis step after step (c), optionally followed by a step of degrading the nucleic acids, and/or
- (ii) a step for inactivating enveloped viruses.

Claim 34 (Previously Presented): The method as claimed in claim 19, wherein said gel filtration chromatography is carried out on a support comprising beads with a diameter of between 10 and 80  $\mu\text{m}$ .

Claim 35 (Canceled).

Claim 36 (Previously Presented): The protocol as claimed in claim 32, wherein said adenoviral vector is a recombinant adenoviral vector.

Claim 37 (Previously Presented): The protocol as claimed in claim 36, wherein said recombinant adenoviral vector is replication defective.

Claim 38 (Currently Amended): A protocol for producing adenoviral particles, comprising:

- (i) producing a crude viral preparation by a procedure comprising:

- (a) infecting or transfecting a suitable cell line with at least one recombinant adenoviral vector;
- (b) culturing said infected or transfected cell line under conditions which allow viral replication and the production of viral particles;
- (c) collecting the cells and/or the supernatant,
- (ii) lysing the cells and/or the supernatant collected at step (i)(c) by mechanical action,
- (iii) clarifying the lysate obtained at step (ii) by successive filtrations to remove the insoluble matter,
- (iv) degrading the nucleic acid in the clarified lysate obtained in step (iii) by the action of benzonase and concomitantly inactivating the enveloped viruses by the action of a mixture of ~~TNBP~~ tributylphosphate and polysorbate 80,
- (v) purifying said adenoviral particles from the viral preparation obtained at step (iv) according to the method of claim 19 further comprising concentrating the adenoviral particles collected in the fluidized bed chromatography step by ~~diafiltration~~before diafiltration before submitting the concentrated adenoviral particles to the gel filtration chromatography step, and
- (vi) sterilizing the adenoviral particles collected at step (v).